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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,638	12/08/2000	Andreas Castan	10806-151	2602

24256 7590 07/25/2002

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EXAMINER

SISSON, BRADLEY L

ART UNIT PAPER NUMBER

1634

DATE MAILED: 07/25/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/732,638

Applicant(s)

CASTAN, ANDREAS

Examiner

Bradley L. Sisson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 May 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 and 22-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 and 22-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Group 1630, Art Unit 1634.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 May 2002 has been entered.

Claim Rejections - 35 USC § 102/103

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in

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section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459

(1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1, 2, 4, 5, 9, 11, 22, 23, and 28 ~~are 28~~ are rejected under 35 U.S.C. 102(a), (e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Nakamura et al. B18

7. Nakamura et al., (US Patent 5,912,113) disclose a method of culturing microorganisms in a batch culture, under aerobic environment whereby glucose is added to the culture media in an oscillating manner. As seen in the abstract as well as at column 10, the time between which glucose is added to the culture media can be less than 2 minutes as well as less than or equal to 30 minutes. Such a teaching is considered to meet the limitation that "the oscillation amplitude has a wave period of from about 1 to about 30 minutes" (claim 1). As seen in the examples,

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yeast as well as bacterial cultures were used. Such a showing meets the limitation that the "biological host" be a bacteria, yeast or animal cell.

8. Figure 8 depicts via bar graph the time periods and rate of glucose addition, which takes on a square wave while the line graph depicts glucose concentration, which takes on a sinus wave pattern. Such a showing is considered to meet the limitations of the waves being characterized as either square or sinus. Additionally, the oscillation feed is considered to have a wave amplitude that ranges from +/- 5% to +/-60% of standard. This meets a limitation of claim 23.

9. Claims 1-5, 8-12, 22, 23, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura et al., (US Patent 5,912,113) in view of Gschaedler et al. (Biotechnology and Bioengineering, Vol. 63, No. 6, June 20, 1999).

10. Nakamura et al., (US Patent 5,912,113) disclose a method of culturing microorganisms in a batch culture, under aerobic environment whereby glucose is added to the culture media in an oscillating manner. As seen in the abstract as well as at column 10, the time between which glucose is added to the culture media can be less than 2 minutes as well as less than or equal to 30 minutes. Such a teaching is considered to meet the limitation that "the oscillation amplitude has a wave period of from about 1 to about 30 minutes" (claim 1). As seen in the examples, yeast as well as bacterial cultures were used. Such a showing meets the limitation that the "biological host" be a bacteria, yeast or animal cell.

11. Figure 8 depicts via bar graph the time periods and rate of glucose addition, which takes on a square wave while the line graph depicts glucose concentration, which takes on a sinus

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wave pattern. Such a showing is considered to meet the limitations of the waves being characterized as either square or sinus. Additionally, the oscillation feed is considered to have a wave amplitude that ranges from +/- 5% to +/-60% of standard. This meets a limitation of claim 23.

12. Nakamura et al., do not teach using *Escherichia coli* in their culturing method.

13. Gschaedler et al., disclose culturing *E. coli* where a recombinant peptide was produced.

14. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to have modified the method of Nakamura et al., so that a different bacterial culture, i.e., one comprising *E. coli* was used in the production of a recombinant peptide as the use of *E. coli* has been and continues to be of biotechnological interest. In view of the well-characterized properties of the microbe, its demonstrate ability to produce a variety of recombinant peptides, the ordinary artisan would not only have been highly motivated to have used this microbe, but would have had a reasonable expectation of success.

15. Claims 6, 7, 13-20, 26, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura et al., and Gschaedler et al., as applied to claims 1-5, 8-12, 22, 23, and 28 above, and further in view of Honjo et al. (US Patent 5,824,502).

16. See above for the basis of the rejection as it pertains to the disclosures of Nakamura et al., and Gschaedler et al.

17. Neither Nakamura et al., nor Gschaedler et al., disclose the recombinant production of a growth hormone, including human growth hormone.

18. Honjo et al., disclose at length the recombinant production of human growth hormone (rhGH).

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19. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to have modified the method of Nakamura et al., such that one would have achieved increased recombinant production of human growth hormone in *E. coli* as rhGH continues to be of great interest and the ability to increase production with less associated costs would have been highly motivating. In view of the well-developed state of rhGH production in *E. coli*, the ordinary artisan would have had a most reasonable expectation of success.

20. Claims 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura et al., and Gschaedler et al., as applied to claims 1-5, 8-12, 22, 23, and 28 above, and further in view of Bhattacharya et al., (Enzyme and Microbial Technology 20:355-360, 1997) and Takahashi et al. (US Patent 5,399,771).

21. See above for the basis of the rejection as it pertains to the disclosures of Nakamura et al., and Gschaedler et al.

22. Neither Nakamura et al., nor Gschaedler et al., disclose varying the speed of stirring the culture.

23. Bhattacharya et al., teach explicitly of the significance on maintaining certain levels of dissolved oxygen and that oxygen levels played a critical role in increased recombinant peptide production in *Escherichia coli*.

24. Bhattacharya et al., do not teach varying the level of stirring but that different constant levels of stirring were employed (Table 1).

25. Takahashi et al., teach explicitly of the need to vary the speed at which a culture is stirred such that the dissolved oxygen level stays at the appropriate level.

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26. While Takahashi et al., do not teach explicitly of varying the stirring speed such that it was +/- 20% of standard, such a limitation is considered to be the result of routine experimentation in view of the prior art teaching explicitly of the need to vary the stirring speed so as to maintain the appropriate dissolved oxygen level in the culture.

27. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to have modified the method of Nakamura et al., and Gschaedler et al., as presented above, with that aspect of varying the speed at which a culture is stirred for as shown by Bhattacharya et al., increased production of recombinant peptide was achieved by maintaining appropriate dissolved oxygen levels. And that said dissolved oxygen level can be achieved through variation in stirring speed (Takahashi et al.). For the above reasons, and in the absence of convincing evidence to the contrary, the claimed invention is considered to be obvious over the combined teachings of the prior art of record.

Conclusion

28. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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29. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

31. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

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32. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
July 20, 2002